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## REMARKS / ARGUMENTS

This Amendment is submitted in response to the final office action dated November 12, 2003, in connection with the above-identified application. A Notice of Appeal is being filed concurrently herewith.

Claims 1-27 are currently pending. Applicant respectfully requests that Claims 1, 2, 3 and 13 be amended. Applicant also respectfully requests the Claim 12 be cancelled without prejudice. Applicant reserves the right to prosecute this Claim at a later date. Thus, Claims 1-11 and 13-27 are currently pending.

### A. Rejections Under 35 U.S.C. 112, Second Paragraph

The Examiner has rejected Claims 1-11 under 35 U.S.C. 112, Second Paragraph as being based on a disclosure which is not enabling. Specifically, the Office Action states, "the 'active substance' is critical or essential to the practice of the invention, but not included in the claim is not enabled by the disclosure [sic]. Step (a) (2) does not require the present [sic] of active substance."

Applicant respectfully disagrees with the Examiner's assertion. The language of Claim 1 relates to the following scenarios:

(I) all of the active is powdered/granulated [step (a)(1)] and dispensed in an auxiliary solvent [(b)(1)];

(II) part of the active is powdered/granulated [step (a)(1)] and dispensed in a solution/dispersion of the remainder of the active in an auxiliary solvent [(b)(2)];

(III) the other pharmaceutical ingredients are powdered/granulated [(a)(2)] and dispensed in solution /dispersion of total of active in auxiliary solvent [(b)(2)].

The preamble in Claim 1 states the requirement of an active substance, in order for a skilled artisan to practice Claim 1 when starting, for example, with "other pharmaceutical ingredients", she has to follow step [(a)(2)] with step [(b)(2)] not [(b)(1)] to add in the active substance. Thus, Applicant disagrees with the Examiner's assertion that step [(a)(2)] does not require an active substance.

The Examiner has rejected Claims 1-11 under 35 U.S.C. 112, Second Paragraph as being based indefinite. Specifically, Claim 1 is rejected because of insufficient antecedent basis for the term "the other ingredients." Applicant has amended this term to read as "the other pharmaceutical ingredients" which does have antecedent basis.

Claim 1 is rejected in the use of step [(a)(2)]. Applicant respectfully submits that the active substance is ultimately present in the invention regardless of whether a skilled artisan begins with step [(a)(1)] or step [(a)(2)]. Applicant respectfully refers the Examiner to the aforementioned remarks.

It is respectfully submitted that this rejection is overcome and should be withdrawn.

**B. Rejections Under 35 U.S.C. 102**

Claims 12-26 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/38679 to Humbert-Droz et al. (hereinafter "*Humbert*"). The Examiner states that *Humbert* teaches fast disintegrating oral dosage forms comprising active agent, filler, binding agent (disintegration agent), and talc as lubricant. Applicant respectfully notes the cancellation without prejudice of Claim 12. Applicant respectfully submits that *Humbert* fails to include the disintegration agents disclosed in Claim 13.

The CAFC has repeatedly stated that "it is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 2131 USPQ 81 (Fed. Cir. 1986). In the present case, this axiom is not met.

Applicant submits that binding agents and disintegration agents have different purposes and are not the same compounds, thus, not being interchangeable. The purpose for which these ingredients are included differentiates these agents. A binder is an agent that holds the ingredients together as a solid dosage form (*e.g.*, a tablet). In contrast, a disintegration agent helps in the rapid disintegration of the tablet when the tablet is administered.

Claim 13 has been amended such that the disintegration agent is "selected from the group consisting of croscarmellose Na, sodium glycolates of starches, cross-linked poly-N-vinyl-2-pyrrolidones, polymethylmethacrylates, soy polysaccharides and synthetic resins." Support for "soy polysaccharides" can be found in the recitation of EMCOSOY on page 11 of the Specification. EMCOSOY from JRS Pharma LP is soy polysaccharides (a copy of literature disclosing EMCOSOY is submitted herewith).

In view of the fact that the *Humbert* fails to teach each and every element of the claimed invention, it is respectfully submitted that Claim 13 and its dependent claims are in condition for allowance. Applicant respectfully requests that this rejection be withdrawn.

**C. Rejections under 35 U.S.C. 103**

Claims 1-27 are rejected under 35 U.S.C. 103 as being unpatentable over *Humbert*.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claimed limitations. *See*, *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

With respect to the method claims, the Examiner stated that *Humbert* is silent as to the teaching of compacting a suitable amount of the prepared powder or granulate, but the extra step does not impart patentability over the prior art. The Examiner states there is no criticality seen in this particular step. Applicant respectfully submits that the Examiner has not established a *prima facie* case of obviousness because *Humbert* is indeed silent regarding the compacting of a suitable amount of the prepared powder or granulate.

Applicants respectfully submits that the present invention not only accomplishes a rapidly dissolving oral dosage form, but also a rapidly dissolving oral dosage form that overcomes many problems associated with drying suspensions that are filled in blister packs. For example, page 2 of the Specification states these problems that are overcome by the specific manufacturing process of the present invention which includes the unique compacting step:

(a) assuring that the dosage forms always have a uniform content of the active ingredient(s);

(b) assuring that the dosage forms always have a uniform table weight (e.g. dose weights accurate within 2-3%);

(c) avoiding a time-consuming process for removing high quantities of solvent;

(d) allowing easy upscaling of the process developed the laboratory; and

(e) avoiding moisture uptake during storage."

These aforementioned clear and unexpected advantages are not taught or suggested by *Humbert*.

Thus, Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness, it is respectfully submitted that this rejection is overcome and should be withdrawn.

**D. Obviousness Type Double Patenting Rejection**

Claims 12-26 are rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,083,531 the ("'531 Patent"). For clarification purposes, Applicant notes that *Humbert* is the PCT priority document of the '531 Patent.

As discussed before, the composition claims of the present invention are significantly different from that of Humbert. The disintegration agents disclosed in Claim 13, *i.e.*, croscarmellose Na, sodium glycolates of starches, cross-linked poly-N-vinyl-2-pyrrolidones, polymethylmethacrylates, soy polysaccharides and synthetic resins, are distinctly and chemically distinct from the binding agents disclosed in *Humbert*. Accordingly, the claims of the present invention are not obvious since the compositions are not identical.

Thus, it is respectfully submitted that this rejection be withdrawn.

Respectfully submitted,

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**Appendix**

Literature regarding EMCOSOY from JSR Pharma

JRS PHARMA JRS LEADING THE WORLD IN EXCIPIENTS



Let's Talk About

# Disintegrants

With nine disintegrant products, JRS Pharma offers you the broadest, most innovative s we created the Super Disintegrant category. But even more significant, we have the disi excipient expertise to help you achieve formulation development success.

Did you know . . . ?

- Explotab® used at high levels can serve as a sustained release matrix.
- There's an all natural Super Disintegrant called Emcosoy.
- Combining disintegrants can produce unique dissolution profiles.

Explotab® and VivaStar® brands of Sodium Starch Glycolate are best in class super d "swelling" or the accelerated absorption of water leading to an enormous increase in th promote disintegration.

| PRODUCT | DESCRIPTION | API |
|---|---|---|
| Explotab & VivaStar P | Sodium Starch Glycolate NF JPE Type A Ph Eur BP | Direct Compr |
| Explotab GL | Sodium Starch Glycolate NF JPE Type A Ph Eur BP | Granulations |
| Explotab Low pH | Sodium Starch Glycolate NF JPE Type A Ph Eur BP | For actives s |
| Explotab V | Sodium Starch Glycolate | For enhance |
| VivaStar (SF) | Sodium Starch Glycolate NF JPE Type A Ph Eur BP | Solvent Free |

Vivasol® Croscarmellose Sodium is a starch-free super disintegrant that adds excelle disintegration.

Emcosoy® (Soy Polysaccharides) is an all natural super disintegrant, which does not Being a dietary fiber, it has excellent application in nutritional products.

JRS Pharma LP

# EMCOSOY STS IP®

*(Soy Polysaccharides)*

## *DESCRIPTION:*

Emcosoy® STS IP[1], Soy Polysaccharides, is an all-natural, soft white to light-tan powder, which does not contain starch or sugar. It is derived from dehulled and defatted soybean flakes by a special process.

Emcosoy® STS IP is a kosher product and is manufactured without the use of bleaching agents. Emcosoy® STS IP typically has 75% dietary fiber with the main components including five types of higher polysaccharides: cellulose, hemicellulose, pectin, gum and mucilage. It is ideally suited for low calorie (2 kcal/g) and diabetic applications.

Emcosoy® STS IP is manufactured from soy that has not been genetically modified. The raw material used in producing Emcosoy® STS IP is segregated during harvesting and processing, and extra control are in place to ensure that such material remains segregated. Additional testing is used to test for the absence of modified gene expression. The soy used is one particular strain (STS) and ther material is termed Identity Preserved (IP).

## *APPLICATIONS AND USES:*

Emcosoy® STS IP exhibits excellent disintegration and improved dissolution characteristics when tablets are prepared by direct compression. Its use in soluble systems has evidenced fast and efficient disintegration of tablets prepared with a broad range of hardness values.

In most formulations, optimum concentration is approximately 6%. This may be modified to meet the disintegration/dissolution requirements of any particular formulation when incorporated in the range of 4% - 10%.

This non-ionic product contains very low concentrations [less than 5.0%] of soluble carbohydrates. This means that the amount of carbohydrates that is metabolized and thus can affect blood sugar levels is very small. For this reason the use of Emcosoy® STS IP in products intended for use by diabetics is considered safe. It is generally recognized as safe (GRAS) and is produced in conformance with current good manufacturing practices for (cGMP) human foods.

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[1] Emcosoy STS IP® STS IP is a registered trademark of JRS Pharma (Rettenmaier)



US Office: Phone 845-878-3414 • 1-800-431-2457 • Fax 845-878-3484
UK Office: Phone +44 1737 222323 • Fax +44 1737 222545

## JRS Pharma LP

# EMCOSOY STS IP®

*(Soy Polysaccharides)*

## *PRODUCT SPECIFICATIONS:*

| | |
|---|---|
| 1. Appearance | Soft, white to light-tan powder |
| 2. pH | 6.5 - 7.5 |
| 3. Residual soy lipids | Not more than 2.0% |
| 4. Moisture | Not more than 8.0% |
| 5. Ash | Not more than 6.0% |
| 6. Heavy metals | Not more than 10 ppm |
| 7. Protein | Not more than 16.0% (on a moisture-free basis) |
| 8. Residual sulfites | Not more than 25 ppm |
| 9. Arsenic | Not more than 1 ppm |

Residual soy lipids, residual sulfites, and arsenic tests: Results shown represent expected limits based on historical product data. JRS Pharma warrants that this material, if tested, will conform to the specification listed for each test.

## *MICROBIOLOGICAL SPECIFICATIONS:*

| | |
|---|---|
| 1. Total aerobic microbial count | Not more than 1000/g |
| 2. Coliforms | Not more than 10/g |
| 3. Escherichia coli | Absent in 25 g |
| 4. Salmonella species | Absent in 100 g |
| 5. Total combined yeasts and molds | Not more than 100/g |

## *PACKAGING:*

Emcosoy® STS IP is available in 20 kg polyethylene-lined bags.



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JRS Pharma LP

# EMCOSOY STS IP®

*(Soy Polysaccharides)*

## *STORAGE RECOMMENDATIONS:*

Emcosoy® STS IP should be stored in original, unopened, well-closed containers under conditions that do not typically exceed 30°C and 70% RH. When stored as recommended, Emcosoy® STS IP has a recommended re-evaluation period of three (3) years from the date of manufacture. An additional year can be added if the Moisture and pH re-evaluation tests are within specification.

## *ADDITIONAL TECHNICAL INFORMATION:*

Chemical Abstract Service [CAS] Registry number: 68513-95-1
Brussels Nomenclature number: 2304 00 00 00
Emcosoy® STS IP Drug Master File number: pending

Although it is generally believed that protein-containing products contribute to the growth of microorganisms, Emcosoy® STS IP does not support such growth. It is reported that water activity values of 0.88% and 0.75% are required to promote bacterial and mold growth respectively. Since moisture contents of 10% and 20% are equivalent to water activity of 0.5% and 0.88% respectively, no possibility of microbial growth exists.

Although phytic acid and phytates may be present in certain cereal grains, including soybean and other soy products, none have been detected in Emcosoy® STS IP.

The protein content of Emcosoy® STS IP is very low and the amounts that can be fed to laboratory animals are small; therefore, it is not feasible to determine the protein efficiency ratio.

Although Emcosoy® STS IP contains no starch, it does produce a blue color with dilute iodine/potassium iodide solution. There are numerous references in the literature to the reaction of higher polysaccharides with iodine to give blue-colored complexes [amyloid reaction]. This reaction forms the basis for separation of individual polysaccharides from the mixtures. [Nature. Vol. 191 September 23, 1961].

## *WARRANTY:*

The information contained in this document is believed to be accurate at the time of issuance and is offered in good faith, with no assumption of liability on the part of JRS Pharma, as a guide to the use and testing of the material, but in no way does this information constitute a performance warranty. JRS Pharma excipients are sold with the understanding that purchasers will determine the suitability of the excipients for their particular applications or purposes.



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